Long-term prognostic value of left ventricular dyssynchrony assessment by phase analysis from myocardial perfusion imaging

Pazhenkottil, A P ; Buechel, R R ; Husmann, L ; Nkoulou, R N ; Wolfrum, M ; Ghadri, J R ; Kummer, J ; Herzog, B A ; Kaufmann, P A

Abstract: OBJECTIVE: To assess the value of left ventricular (LV) dyssynchrony, using phase analysis of nuclear single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) as independent predictor of cardiac events. METHODS: Phase analysis using Emory Cardiac Toolbox was applied on gated rest MPI scans to assess LV dyssynchrony in a total of 202 patients. Follow-up was obtained in 197 patients (97.5%). Major adverse cardiac events (MACE) (cardiac death and hospitalisation for any cardiac reasons, including worsening of heart failure, non-fatal myocardial infarction, unstable angina and coronary revascularisation) were determined using the Kaplan-Meier method. Cox proportional hazard regression was used to identify independent predictors of cardiac events. RESULTS: At a median follow-up of 3.2 ± 1.2 years, 41 patients had at least one event, including 5 cardiac deaths. LV dyssynchrony (n = 35) was associated with a significantly higher incidence of MACE ($p<0.001$) and proved to be an independent predictor of cardiac events. CONCLUSION: LV dyssynchrony assessed by phase analysis of gated SPECT-MPI is a strong predictor of MACE independent of other known predictors such as perfusion defects or decreased LV ejection fraction.

DOI: https://doi.org/10.1136/hrt.2010.201566

Heart Online First, published on October 20, 2010 as 10.1136/hrt.2010.201566

Long-term prognostic value of left ventricular dyssynchrony assessment by phase analysis from myocardial perfusion imaging

Aju P Pazhenkottil,[1] Ronny R Buechel,[1] Lars Husmann,[1] René N Nkoulou,[1] Mathias Wolfrum,[1] Jelena-Rima Ghadri,[1] Janine Kummer,[1] Bernhard A Herzog,[1] Philipp A Kaufmann[1,2]

[1]Cardiac Imaging, University Hospital Zurich, Zurich, Switzerland
[2]Zurich Center for Integrative Human Physiology (ZIHP), University of Zurich, Switzerland

Correspondence to
Philipp A Kaufmann, Cardiac Imaging, University Hospital Zurich, Ramistrasse 100, CH-8091 Zurich, Switzerland; pak@usz.ch

Accepted 16 August 2010

ABSTRACT

Objective To assess the value of left ventricular (LV) dyssynchrony, using phase analysis of nuclear single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) as independent predictor of cardiac events.

Methods Phase analysis using Emory Cardiac Toolbox was applied on gated rest MPI scans to assess LV dyssynchrony in a total of 202 patients. Follow-up was obtained in 197 patients (97.5%). Major adverse cardiac events (MACE) (cardiac death and hospitalisation for any cardiac reasons, including worsening of heart failure, non-fatal myocardial infarction, unstable angina and coronary revascularisation) were determined using the Kaplan–Meier method. Cox proportional hazard regression was used to identify independent predictors of cardiac events.

Results At a median follow-up of 3.2±1.2 years, 41 patients had at least one event, including 5 cardiac deaths. LV dyssynchrony (n=35) was associated with a significantly higher incidence of MACE ($p<0.001$) and proved to be an independent predictor of cardiac events.

Conclusion LV dyssynchrony assessed by phase analysis of gated SPECT-MPI is a strong predictor of MACE independent of other known predictors such as perfusion defects or decreased LV ejection fraction.

INTRODUCTION

In Western countries, congestive heart failure is a major cause of morbidity and mortality. Great efforts have been made to search for optimised treatment. The combination of cardiac resynchronisation therapy (CRT) with standard pharmacological treatment is a widely used method for the treatment of patients with moderate to severe heart failure (New York Heart Association functional class III–IV, reduced left ventricular ejection fraction (LVEF) ≤35% and a broad QRS complex >120 ms).[1–3] It has been shown that left ventricular (LV) dyssynchrony is a good predictor of therapeutic response to CRT in those patients.[4] Several non-invasive imaging methods, such as tissue Doppler imaging, multigated blood pool ventriculography acquisition (MUGA), MRI and nuclear imaging, have been developed for the accurate assessment of LV dyssynchrony. Among these, MUGA has for long time represented the most accurate and reproducible technique.[5] Recently, phase analysis of gated single-photon emission computed tomography myocardial perfusion imaging (SPECT-MPI) using Fourier harmonic function has been introduced as a reliable alternative for LV dyssynchrony assessment.[6 7]

Although the pathophysiology of heart failure has been well investigated and the outcome of intra-left ventricular dyssynchrony has been documented in patients with heart failure,[8] there is still a lack of knowledge about the outcome value of intra-left ventricular dyssynchrony assessed by gated SPECT-MPI in an unselected population. Hence, the purpose of this study was to assess the prognostic value of LV dyssynchrony assessed from phase analysis of SPECT-MPI as an independent predictor of future cardiac events.

MATERIALS AND METHODS

The study included a total of 202 consecutive patients who underwent a 1-day adenosine stress/rest SPECT-MPI on a standard dual-detector SPECT camera (Ventri, GE Healthcare, Milwaukee, Wisconsin) for evaluation of known or suspected coronary artery disease (CAD) and who were in sinus rhythm during scanning. A weight-adjusted dose of 300–400 MBq ^{99m}Tc-tetrofosmin was injected at stress, followed by a threefold higher dose at rest. The latter (high dose) scan was used for phase analysis. The study protocol was approved by the institutional review board (local ethics committee of the University Hospital Zurich) and written informed consent was obtained from each patient.

Image acquisition and reconstruction

The SPECT-MPI acquisition was performed on a Ventri dual-head camera with a low-energy, high-resolution collimator, a 20% symmetric window at 140 keV, a 64×64 matrix and an elliptic orbit with step-and-shoot acquisition at 3° intervals over 180° arc (45° right anterior oblique to 45° left posterior oblique) with 30 steps (60 views). Scan time was set to 25 s per frame for stress and rest, resulting in a total acquisition time of 14 min 52 s (including inter-step rotation time) for each scan as recommended by the American Society of Nuclear Cardiology.[9] Images were reconstructed on a dedicated workstation using a standard iterative reconstruction algorithm with ordered subset expectation maximisation with two iterations and 10 subsets into standard short as well as vertical and horizontal long-axis and polar maps of perfusion encompassing the entire left ventricle without using resolution compensation or attenuation correction.

Image interpretation

Image interpretation was visually performed in consensus by two nuclear cardiologists—both of whom were blinded to the clinical history and to the findings from phase analysis—on short-axis, horizontal long-axis and vertical long-axis sections and semiquantitative polar maps of perfusion as previously reported.[10] Reversible perfusion defect, fixed perfusion defect and partially reversible defect were defined as abnormal perfusion. Summed rest, stress and difference scores were calculated based on a 20-segment model as previously reported.[11] Ejection fraction was determined from gated SPECT. An ejection fraction <50% was defined as abnormal.[12]

Phase analysis

Phase analysis of Emory Cardiac Toolbox software[6] (Emory University/ Syntermed, Atlanta, Georgia, USA) was used to evaluate the gated SPECT images obtained from Ventri. The phase analysis technique measures the first Fourier harmonic phase of regional LV count changes throughout the cardiac cycle, which is approximately linear to the myocardial wall thickness and therefore related to the time interval when a region in the LV myocardial wall starts to contract. It provides information on regularity of the distribution of these time intervals for the entire left ventricle—that is, it is a measure of LV synchrony or dyssynchrony (figure 1).[4 6 7 13] The following two parameters obtained from the phase analysis were evaluated, as they have been shown to best identify LV dyssynchrony[7 14]: (1) phase histogram bandwidth; (2) phase histogram standard deviation (SD). The previously established normal values[6] were 38.7°±11.8° (men) and 30.6°±9.6° (women) for histogram bandwidth and 14.2°±5.1° (men) and 11.8°±5.2° (women) for phase SD. LV dyssynchrony was defined as greater than the mean + 2 standard deviations. LV dyssynchrony was considered to be present if at least one of the parameters was above the cut-off value. All analyses were performed by a reader who was blinded to the history of the patient.

Long-term follow-up

Patient follow-up was accomplished by obtaining a structured interview, and a clinical history assessed by a phone call to all patients and/or general practitioners or cardiologists. Additional information was gathered from medical charts and the registry of government authorities in cases of death.

The median follow-up was 3.2±1.2 years. The date of the last examination or consultation was used to determine follow-up. The following major adverse cardiac events (MACE) were defined as end points: cardiac death (as declared in the medical charts) and hospitalisation for any cardiac reason, including worsening of heart failure (as defined by the ESC guidelines),[15] non-fatal myocardial infarction (as defined by the joint ESC/ACCF/AHA/WHF consensus definition),[16] unstable angina and coronary revascularisation. All revascularisations during the first

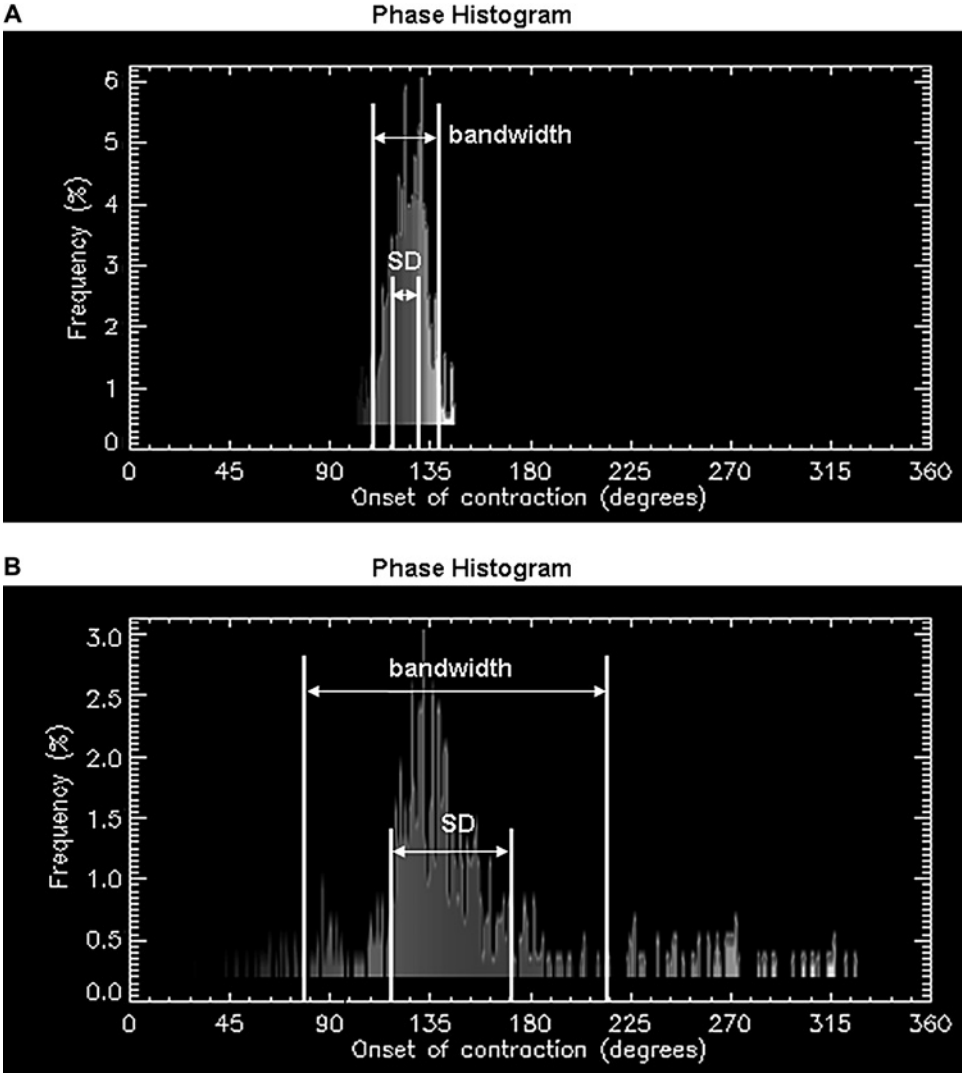

Figure 1 Phase histograms of a patient without (A) and a patient with left ventricular dyssynchrony (B). In the latter histogram bandwidth and SD are enlarged.

30 days were excluded because during this period any revascularisation could potentially be directly triggered by the MPI test result, which would introduce a confounder between diagnostic and prognostic value.

Statistical analysis

SPSS software (SPSS 15.0, SPSS Inc) was used for statistical testing. Quantitative variables were expressed as mean ± standard deviation and categorical variables as frequencies or percentages. Differences between the patient population with and without LV dyssynchrony were tested for significance using χ^2 tests for comparison of cross tables. For further comparison, Mann–Whitney U-tests were performed for age, body mass index and LVEF. χ^2 Tests were used to determine differences in gender, coronary risk factors and prevalence of known CAD.

Differences in survival over time were analysed by the Kaplan–Meier method. The log-rank test was used to compare the survival curves. Univariate and multivariate Cox proportional hazard regression models were used to identify independent predictors of cardiac events. Variables were selected in a stepwise forward selection manner; entry and retention sets with $p < 0.05$ were considered to indicate a significant difference. Variables included in the models were age, male gender, more than two risk factors (ie, hypertension, hypercholesterolaemia, smoking, diabetes mellitus, a positive family history of CAD), LV dyssynchrony, abnormal perfusion and abnormal ejection fraction. A variable's risk was expressed as the hazard ratio with corresponding 95% confidence interval. p Values of <0.05 were considered statistically significant.

RESULTS

In 202 patients phase analysis of Emory Cardiac Toolbox was applied using rest MPI scans in order to assess LV dyssynchrony. Follow-up was successful in 197 patients (97.5%). Baseline characteristics of the study population are given in table 1. ECG signs of ischaemic heart disease were present in 22 patients, of whom 10 had LV dyssynchrony. QRS >120 ms was present in 15 patients, of whom six had LV dyssynchrony. All other patients had normal ECG.

SPECT-MPI findings and phase analysis

Phase analysis disclosed LV dyssynchrony in 35 patients. Of these, 31 patients had an abnormal histogram bandwidth and 26 patients an abnormal SD. In 22 patients both parameters were abnormal. A total of 67 patients had an abnormal perfusion; mean values for summed rest, stress and difference scores were 3.9±5.6, 9.6±8.4 and 5.5±5.5, respectively. An abnormal ejection fraction was found in 69 patients.

Table 1 Baseline characteristics of the study population (n=197)

	Event-free (n=156)	With events (n=41)	p Value
Characteristics			
Male gender, n (%)	108 (69.2)	29 (70.7)	NS
Age (years)			
mean±SD, range	62±11, 33–88	65±10, 44–86	NS
Body mass index (kg/m2)			
mean±SD, range	26.8±4.8, 18.7–50.0	28.2±5.0, 20.3–47.5	<0.05
Ejection fraction (%)			
mean ± SD, range	60.8±12.0, 19–84	58.0±12.4, 28–78	NS
Risk factors, n (%)			
Hypertension	94 (60.3)	31 (75.6)	NS
Dyslipidaemia	67 (42.9)	25 (61.0)	<0.05
Diabetes	27 (17.3)	10 (24.4)	NS
Smoking	45 (28.8)	20 (48.8)	<0.05
Positive family history	40 (25.6)	17 (41.5)	<0.05
Known CAD, n (%)	24 (15.4)	11 (26.8)	NS

CAD, coronary artery disease.

Table 2 Major adverse cardiac events (MACE) in different groups

	Patients without LV dyssynchrony (n=162)	Patients with LV dyssynchrony (n=35)	All patients (n=197)
MACE			
Cardiac death	4	1	5
Non-fatal myocardial infarction	5	2	7
Hospitalisation for any cardiac reason	31	19	50
All MACE	40	22	62

LV, left ventricular.

Outcome data

During 3.2±1.2 years of follow-up, 62 MACE occurred in 41 patients, including five cardiac deaths (table 2). The Kaplan–Meier survival curves revealed a significantly higher rate of MACE ($p<0.001$) in patients with LV dyssynchrony than in those without (figure 2). Similarly, patients with abnormal perfusion and/or abnormal LVEF have a significantly higher rate of MACE ($p<0.001$ and $p<0.05$). The predictive values of LV dyssynchrony, abnormal perfusion and abnormal LVEF proved to be significant by univariate Cox regression analysis (table 3). In addition, there was a tendency for a higher annualised MACE rate in those patients above versus those below the median value of LV dyssynchrony (21.9% vs 16.6%), although this difference fell short of statistical significance.

Moreover, by multivariate Cox regression analysis, three independent predictors of MACE were identified: LV dyssynchrony, the presence of more than two risk factors and abnormal myocardial perfusion were independent predictors of MACE (table 3).

DISCUSSION

Our results demonstrate an added prognostic value of LV dyssynchrony assessed by SPECT-MPI over other known predictors such as perfusion abnormalities and decreased LVEF. It

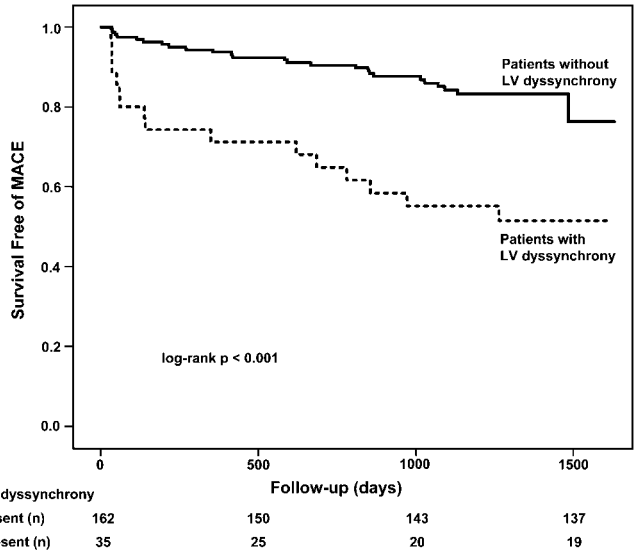

Figure 2 Left ventricular (LV) dyssynchrony predicts major adverse cardiac events (MACE).

Table 3 Predictors of events at univariate and multivariate analysis (n = 197)

Predictors	Univariate HR (95% CI)	p-value	Multivariate HR (95% CI)	p Value
Clinical characteristics				
Age	1.033 (1.002 to 1.065)	<0.05	1.029 (0.546 to 1.939)	NS
Male gender	1.146 (0.584 to 2.247)	NS	0.796 (0.392 to 1.618)	NS
Cardiovascular risk factors				
>2 Risk factors	2.172 (1.176 to 4.010)	< 0.05	1.906 (1.023 to 3.548)	<0.05
LV dyssynchrony	3.626 (1.932 to 6.803)	< 0.001	2.049 (1.004 to 4.179)	<0.05
Abnormal perfusion	3.895 (2.077 to 7.306)	< 0.001	2.872 (1.416 to 5.826)	<0.01
Abnormal LVEF	2.196 (1.190 to 4.053)	< 0.05	1.315 (0.638 to 2.711)	NS

CI, confidence interval; HR, hazard ratio; LVEF, left ventricular ejection fraction.

has been demonstrated earlier that ventricular dyssynchrony is a predictor of poor outcome in patients with heart failure and in patients with idiopathic dilated cardiomyopathy.[8 17] To our knowledge, our study is the first to show the prognostic value of LV dyssynchrony assessed by phase analysis of gated SPECT in an unselected population.

The results of this study are in line with other studies showing that the presence of intra-LV dyssynchrony is an independent predictor of MACE in patients with heart failure, extending these findings to an unselected non-heart failure population.[8 17 18]

As heart failure has become one of the leading causes of morbidity and mortality in Western countries, the role of diagnostic assessment and treatment of heart failure has gained importance. So far, CRT in addition to medical treatment has been used in patients with severe heart failure and a broad QRS complex. Recently, focus has diverged to use CRT in patients with less severe heart failure,[19 20] suggesting that patients with milder symptoms and evidence of LV dyssynchrony may benefit from CRT implantation and achieve an improved quality of life, exercise capacity, morbidity and mortality.

Our results confirm the importance of LV dyssynchrony assessment for predicting long-term outcome. SPECT-MPI is commonly part of the non-invasive management of patients evaluated for potential CRT, and therefore obtaining reliable dyssynchrony assessment from the same test confers an important added value. The accuracy of LV dyssynchrony assessment of SPECT-MPI has been previously validated,[7] and our outcome data confirm the clinical validity of this test.

Several studies have reported refinements of echocardiographic measurements to assess myocardial dyssynchrony, including Doppler interventricular delay calculated as the difference between aortic and pulmonary pre-ejection delay,[21] three-dimensional echocardiography,[22] colour kinesis,[23] or tissue Doppler imaging.[24] Although these methods may provide valuable information on the location and the degree of ventricular dyssynchrony, no prognostic data are available. By contrast, our data document the prognostic value of LV dyssynchrony as assessed by phase analysis from gated SPECT.

LV dyssynchrony assessment with gated SPECT-MPI scans has several potential advantages over other methods, such as the averaged acquisition over several minutes minimising the impact of respiratory or beat-to-beat variability and automated analysis, both providing better reliability and repeatability than echocardiography as well as providing information on myocardial perfusion at the same time. This may, at least in part, explain why LV dyssynchrony assessed from gated SPECT confers strong predictive outcome information. Although our study does not offer mechanistic insights into the way in which dyssynchrony translates into events, one could speculate that there is inhomogeneous flow caused by premature atherosclerosis or endothelial and microvascular dysfunction.

The relation between LV synchronicity and cardiovascular risk factors has been documented earlier.[25 26] It has been shown that synchronicity was impaired in hypertensive patients and in patients with metabolic syndromes. LV dyssynchrony may therefore reflect a possible mechanistic link between cardiovascular risk factors and cardiac events. As one of the most common cause of chronic heart failure is CAD,[27] a widely available comprehensive diagnostic tool such as SPECT-MPI, allowing assessment of both pathologies—that is, ischaemia and dyssynchrony, at the same time, provides a great advantage.

We acknowledge the following limitations: first, the use of a manual base and apex contour placement for phase analysis may theoretically lead to arbitrary bias. However, the superiority of manual placement over automated contour placement has been previously proved.[28] Second, the inclusion of revascularisation in the list of MACE may raise some criticism, because any revascularisation may be triggered by the MPI finding independent of LV dyssynchrony. However, to avoid this confounder we excluded revascularisations within the first 30 days, as within this period revascularisations are typically completed in our institution and interventions beyond this point can be considered as independent events. Despite crossover bias to revascularisation after MPI with ischaemia (probably often linked with LV dyssynchrony, which may artificially improve outcome in patients with dyssynchrony), LV dyssynchrony remains a strong discriminating predictor. Finally, this method provides exclusively data on LV intraventricular dyssynchrony, while other methods (such as echocardiography[29] or MUGA[17]) may provide data on right ventricular and interventricular dyssynchrony. However, our data underline the prognostic value of LV intraventricular dyssynchrony assessment, in line with previous data showing that it is more pertinent to find reliable assessment of intraventricular dyssynchrony, while interventricular delay had no prognostic value.[17] Therefore, intraventricular dyssynchrony has been suggested as the best predictor of CRT response as measured by improved outcome.[17]

In conclusion, this study documents that LV dyssynchrony assessed by phase analysis of gated SPECT-MPI is a strong and independent predictor of MACE.

Acknowledgements We are grateful to Ennio Mueller, Edlira Loga, Mirjam De Bloeme and Désirée Beutel for their excellent technical support.

Funding The study was supported by a grant from the Swiss National Science Foundation.

Competing interests None.

Patient consent Obtained.

Ethics approval This study was conducted with the approval of the local ethics committee of the University Hospital Zurich.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. **Abraham WT,** Fisher WG, Smith AL, *et al*. Cardiac resynchronization in chronic heart failure. *N Engl J Med* 2002;**346**:1845—53.
2. **Bristow MR,** Saxon LA, Boehmer J, *et al*. Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med* 2004;**350**:2140—50.
3. **Cleland JG,** Daubert JC, Erdmann E, *et al*. The effect of cardiac resynchronization on morbidity and mortality in heart failure. *N Engl J Med* 2005;**352**:1539—49.
4. **Henneman MM,** Chen J, Dibbets-Schneider P, *et al*. Can LV dyssynchrony as assessed with phase analysis on gated myocardial perfusion SPECT predict response to CRT? *J Nucl Med* 2007;**48**:1104—11.
5. **Hesse B,** Tagil K, Cuocolo A, *et al*. EANM/ESC procedural guidelines for myocardial perfusion imaging in nuclear cardiology. *Eur J Nucl Med Mol Imaging* 2005;**32**:855—97.
6. **Chen J,** Garcia EV, Folks RD, *et al*. Onset of left ventricular mechanical contraction as determined by phase analysis of ECG-gated myocardial perfusion SPECT imaging: development of a diagnostic tool for assessment of cardiac mechanical dyssynchrony. *J Nucl Cardiol* 2005;**12**:687—95.
7. **Henneman MM,** Chen J, Ypenburg C, *et al*. Phase analysis of gated myocardial perfusion single-photon emission computed tomography compared with tissue Doppler imaging for the assessment of left ventricular dyssynchrony. *J Am Coll Cardiol* 2007;**49**:1708—14.
8. **Bader H,** Garrigue S, Lafitte S, *et al*. Intra-left ventricular electromechanical asynchrony. A new independent predictor of severe cardiac events in heart failure patients. *J Am Coll Cardiol* 2004;**43**:248—56.
9. **Hansen CL,** Goldstein RA, Akinboboye OO, *et al*. Myocardial perfusion and function: single photon emission computed tomography. *J Nucl Cardiol* 2007;**14**:e39—60.
10. **Fleischmann S,** Koepfli P, Namdar M, *et al*. Gated (99m)Tc-tetrofosmin SPECT for discriminating infarct from artifact in fixed myocardial perfusion defects. *J Nucl Med* 2004;**45**:754—9.
11. **Berman DS,** Kang X, Van Train KF, *et al*. Comparative prognostic value of automatic quantitative analysis versus semiquantitative visual analysis of exercise myocardial perfusion single-photon emission computed tomography. *J Am Coll Cardiol* 1998;**32**:1987—95.
12. **Nakajima K,** Kusuoka H, Nishimura S, *et al*. Normal limits of ejection fraction and volumes determined by gated SPECT in clinically normal patients without cardiac events: a study based on the J-ACCESS database. *Eur J Nucl Med Mol Imaging* 2007;**34**:1088—96.
13. **Cooke CD,** Garcia EV, Cullom SJ, *et al*. Determining the accuracy of calculating systolic wall thickening using a fast Fourier transform approximation: a simulation study based on canine and patient data. *J Nucl Med* 1994;**35**:1185—92.
14. **Boogers MM,** Van Kriekinge SD, Henneman MM, *et al*. Quantitative gated SPECT-derived phase analysis on gated myocardial perfusion SPECT detects left ventricular dyssynchrony and predicts response to cardiac resynchronization therapy. *J Nucl Med* 2009;**50**:718—25.
15. **Dickstein K,** Cohen-Solal A, Filippatos G, *et al*. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2008 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association of the ESC (HFA) and endorsed by the European Society of Intensive Care Medicine (ESICM). *Eur Heart J* 2008;**29**:2388—442.
16. **Thygesen K,** Alpert JS, White HD, *et al*. Universal definition of myocardial infarction. *Circulation* 2007;**116**:2634—53.
17. **Fauchier L,** Marie O, Casset-Senon D, *et al*. Interventricular and intraventricular dyssynchrony in idiopathic dilated cardiomyopathy: a prognostic study with fourier phase analysis of radionuclide angioscintigraphy. *J Am Coll Cardiol* 2002;**40**:2022—30.
18. **Aljaroudi WA,** Hage FG, Hermann D, *et al*. Relation of left-ventricular dyssynchrony by phase analysis of gated SPECT images and cardiovascular events in patients with implantable cardiac defibrillators. *J Nucl Cardiol* 2010;**17**:398—404.
19. **Cleland JG,** Freemantle N, Daubert JC, *et al*. Long-term effect of cardiac resynchronisation in patients reporting mild symptoms of heart failure: a report from the CARE-HF study. *Heart* 2008;**94**:278—83.
20. **Linde C,** Abraham WT, Gold MR, *et al*. Randomized trial of cardiac resynchronization in mildly symptomatic heart failure patients and in asymptomatic patients with left ventricular dysfunction and previous heart failure symptoms. *J Am Coll Cardiol* 2008;**52**:1834—43.
21. **Rouleau F,** Merheb M, Geffroy S, *et al*. Echocardiographic assessment of the interventricular delay of activation and correlation to the QRS width in dilated cardiomyopathy. *Pacing Clin Electrophysiol* 2001;**24**:1500—6.
22. **Kim WY,** Sogaard P, Mortensen PT, *et al*. Three dimensional echocardiography documents haemodynamic improvement by biventricular pacing in patients with severe heart failure. *Heart* 2001;**85**:514—20.
23. **Godoy IE,** Mor-Avi V, Weinert L, *et al*. Use of color kinesis for evaluation of left ventricular filling in patients with dilated cardiomyopathy and mitral regurgitation. *J Am Coll Cardiol* 1998;**31**:1598—606.
24. **Garrigue S,** Jais P, Espil G, *et al*. Comparison of chronic biventricular pacing between epicardial and endocardial left ventricular stimulation using Doppler tissue imaging in patients with heart failure. *Am J Cardiol* 2001;**88**:858—62.
25. **Chang SA,** Kim HK, Kim DH, *et al*. Left ventricular systolic and diastolic dyssynchrony in asymptomatic hypertensive patients. *J Am Soc Echocardiogr* 2009;**22**:337—42.
26. **Tan HW,** Zheng GL, Li L, *et al*. Impaired left ventricular synchronicity in hypertensive patients with ventricular hypertrophy. *J Hypertens* 2008;**26**:553—9.
27. **Gheorghiade M,** Bonow RO. Chronic heart failure in the United States: a manifestation of coronary artery disease. *Circulation* 1998;**97**:282—9.
28. **Trimble MA,** Velazquez EJ, Adams GL, *et al*. Repeatability and reproducibility of phase analysis of gated single-photon emission computed tomography myocardial perfusion imaging used to quantify cardiac dyssynchrony. *Nucl Med Commun* 2008;**29**:374—81.
29. **D'Andrea A,** Caso P, Severino S, *et al*. Prognostic value of intra-left ventricular electromechanical asynchrony in patients with hypertrophic cardiomyopathy. *Eur Heart J* 2006;**27**:1311—18.

Long-term prognostic value of left ventricular dyssynchrony assessment by phase analysis from myocardial perfusion imaging

Aju P Pazhenkottil, Ronny R Buechel, Lars Husmann, et al.

Heart published online October 20, 2010
doi: 10.1136/hrt.2010.201566